The Examiner reasons as follows: Groups I-III are deemed to be different in that they are not a product, a process specially adapted for the manufacture of the said product, and a use of the said product. The Examiner states, "the product of Group III (claim 15) [sic, 24] is required to be treated with papain what is not required for neither the product of Group I (claim 1 or claim 12) not the product of Group II (claim 15)".

With respect to the claims of Groups III and IV the Examiner states that the products of these claims "are different products as claimed and they comprises [sic] different tissues suitable for mammalian transplantation such as either tissue treated with enzyme (claim 24) or untreated tissue (claim 27)".

Applicant traverses this requirement and requests consideration of all claims together in this application, for the reasons set forth below.

REMARKS

The common feature of the invention that runs through all of the artificial groups of the restriction relates to methods for preventing the rejection of transplanted live donor tissue by a host organism by treating the donor tissue with an enzyme to temporarily remove MHC Class I antigens from the surface, and therefore the embodiments AS CLAIMED are seen to be properly examined together under 37 C.F.R. §1.475.

The claims are related as a method of preparing a transplant tissue by treatment with an enzyme, in particular papain, and the tissue *per se* that is the product of that method. Specifically, Claims 1-14 (Group I), expressly recite a method for inhibiting transplant rejection by treating donor tissue with an enzyme to temporarily remove MHC Class I antigens prior to transplantation into a host; Claims 15-23 (Group II) relate to a method for preparing the donor tissue for transplantation comprising treatment with an enzyme to temporarily remove MHC Class I antigens from the donor tissue; Claims 24-26 (Group III) relate to the enzyme-treated donor tissue; and Claims 27-37 (Group IV) relate to a transplantation pack (i.e., kit) comprising donor tissue in contact with an enzyme solution to temporarily remove MHC Class I antigens prior to transplantation into a host organism. Therefore, all the claims are related in that they refer to a method for treating a tissue with an enzyme and the tissue treated with the enzyme. In other words, a method for making a product and the product made, in this case, a live donor tissue treated with papain to temporarily deplete the tissue of MHC Class I surface antigens that is suitable for transplantation into a host organism. As such, a search of the claims of any group will reveal all art related to treating donor tissue with an enzyme to temporarily ablate MHC Class I surface antigens prior to transplantation into a host organism.

The Examiner has cited Stone, U.S. Pat. No. 6,110,206 for the proposition that "methods of making enzyme treated donor tissue suitable for transplantation are known in the art". In actuality, the Stone reference teaches one skilled in the art away from the method disclosed in the present application. Specifically, Stone discloses, in a particular embodiment, the killing of the donor tissue prior to transplantation to prevent reexpression of surface antigens and rejection of the transplanted tissue,

> "In one embodiment of this method of the invention, the xenograft is subjected to a cellular disruption treatment to kill the cells of the ligament prior to *in vitro* digestion of the xenograft with glycosidases. Typically after surface carbohydrate moieties have been removed from nucleated cells and extracellular components, nucleated cells, i.e., living cells reexpress the surface carbohydrate moieties. *Reexpression* of antigenic moieties of a xenograft *can provoke continued immunogenic rejection* of the xenograft. In contrast, non-nucleated, i.e., dead cells, are unable to reexpress surface carbohydrate moieties. Removal of antigenic surface carbohydrate moieties from the non-nucleated cells and extracellular components of a xenograft substantially *permanently eliminates* antigenic surface carbohydrate moieties as a source of immunogenic rejection of the xenograft. (See, col. 6, lines 47-61). (emphasis added).

In contrast, the present invention specifically contemplates that the cells of the donor tissue must remain alive and viable,

> "As a practical matter, removal of as much of the MHC Class I antigens as possible *without killing the tissue* is desired . . . At high enzyme concentration, incubation of tissues may be for even shorter periods, so long as the cells *are not damaged.* Since the tissues *must remain viable after transplant*, the treatment must be adjusted so that not too great a percentage of the donor cells are killed during the treatment process . . ." (See, page 5, lines 2-16). (emphasis added).

In addition, also in (sharp) contrast to the teachings of Stone, the present invention specifically contemplates the rejuvenation of the surface MHC Class I molecules in order to "educate" the host to recognize them as "self" antigens,

> "Since the tissues will remain viable after treatment according to this invention, expression of MHC molecules will continue, and eventually *reappearance of MHC antigens* on the donor tissue will occur, e.g., after transplantation . . . *Reappearance of MHC antigens* may be used to advantage for inducing tolerance of the donor graft, through *re-education of the recipient's immune system* to recognize and tolerate the donor antigens as they reappear." (See, page 5, line 32 to page 6, line 8). (emphasis added).

For the reasons set forth above, Applicant respectfully submits that the claims as grouped for restriction by the Examiner do not represent separate or distinct inventions, and the search of

all claims together in one application would not place a serious burden on the Patent Office. Accordingly, withdrawal of the restriction requirement is requested.

Conclusion and Provisional Election

Applicant submits that in view of the foregoing remarks, all the claims are seen to relate to a single inventive concept, and the claims are in a form and are of the sort that is properly viewed as relating to a single invention that should not be restricted under 35 U.S.C. §121 or 35 U.S.C. §372. Applicant earnestly requests that the restriction and election requirements of the Office Action of October 9, 2002 be reconsidered and withdrawn.

Although, for reasons set forth above in detail, Applicant believes that the restriction requirement is improper and uncalled for, and without in any way acquiescing in the reasons for the requirements set forth in the Office Action, but in order to be fully responsive to the Office Action, Applicant provisionally elects for examination the claims of Group I (i.e., Claims 1-14).

Allowance of the claims is respectfully requested.

Respectfully submitted,

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CERTIFICATE OF MAILING

The undersigned hereby certifies that this correspondence is being deposited with the U.S. Postal Service as first class mail, in an envelope addressed to the Commissioner for Patents, Washington, DC 20231, on the date indicated below.

November 19, 2002
date of mailing

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